DIALOG-BIOTECH

```
?s au=hendrickson, w?
      S1     474  AU=HENDRICKSON, W?
?s au=jiang, x?
      S2    5493  AU=JIANG, X?
?s au=langley, k?
      S3     327  AU=LANGLEY, K?
?s au=syed, r?
      S4      64  AU=SYED, R?
?s au=hsu, y?
      S5    2346  AU=HSU, Y?
?s s1 or s2 or s3 or s4
             474  S1
            5493  S2
             327  S3
              64  S4
      S6    6349  S1 OR S2 OR S3 OR S4
?s s6 and scf
            6349  S6
           52286  SCF
      S7      20  S6 AND SCF
?s s7 and strucuture
              20  S7
             178  STRUCUTURE
      S8       0  S7 AND STRUCUTURE
?s s7 and structure
              20  S7
         6765103  STRUCTURE
      S9       4  S7 AND STRUCTURE
```

10/AU,TI,SO,AB/1 (Item 1 from file: 76)

Structure **of the active core of human stem cell factor and analysis of binding to its receptor Kit**
Jiang, X. ; Gurel, O.; Mendiaz, E.A.; Stearns, G.W.; Clogston, C.L.; Lu, H.S.; Osslund, T.D.; **Syed, R.S.** ; **Langley, K.E.** ; **Hendrickson, W.A.**
EMBO Journal vol. 19, no. 13, pp. 3192-3203 (2000)

Stem cell factor (**SCF**) is an early-acting hematopoietic cytokine that elicits multiple biological effects. **SCF** is dimeric and occurs in soluble and membrane-bound forms. It transduces signals by ligand- mediated dimerization of its receptor, Kit, which is a receptor tyrosine kinase related to the receptors for platelet-derived growth factor (PDGF), macrophage colony- stimulating factor, Flt-3 ligand and vascular endothelial growth factor (VEGF). All of these have extracellular ligand-binding portions composed of immunoglobulin-like repeats. We have determined the crystal **structure** of selenomethionyl soluble human **SCF** at 2.2 Aa resolution by multiwavelength anomalous diffraction phasing. **SCF** has the characteristic helical cytokine topology, but the **structure** is unique apart from core portions. The **SCF** dimer has a symmetric 'head-to-head' association. Using various prior observations, we have located potential Kit-binding sites on the **SCF** dimer. A superimposition of this dimer onto VEGF in its complex with the receptor Flt-1 places the binding sites on **SCF** in positions of topographical and electrostatic complementarity with the Kit counterparts of Flt-1, and a similar model can be made for the complex of PDGF with its receptor.

10/AU,TI,SO,AB/2 (Item 2 from file: 76)

Epitope mapping and immunoneutralization of recombinant human stem-cell factor
Mendiaz, E.A.; Chang, D.G.; Boone, T.C.; Grant, J.R.; Wypych, J.; Aguero, B.; Egrie, J.C.; **Langley, K.E.**
EUR. J. BIOCHEM. vol. 239, no. 3, pp. 842-849 (1996)

The epitope regions of three anti-[stem-cell factor (**SCF**)] Ig have been mapped by characterization of immunoreactivities against truncated forms of **SCF** in immunoblots and against synthetic peptides in solution-phase competition ELISA. Two of the antibodies, mAb 7H6 and mAb 8H7A, were raised against Escherichia coli-derived human **SCF** -(1-164) while the third, polyclonal antibody (pAb) 1337, was raised against a peptide corresponding to residues 3-31 of human **SCF** . The epitopes of mAbs 7H6 and 8H7A have been mapped to residues 61-95 and 95-110, respectively. The epitope of pAb 1337 has been mapped to residues 21-31. The ability of the anti- **SCF** Ig to recognize E. coli-derived human **SCF** presented in various formats, i.e. partially denatured (fixed in standard ELISA or on a western blot) or native (in solution), was studied. mAb 7H6 recognized its epitope in partially denatured or native **SCF** with equally high affinity, while mAb 8H7A and pAb 1337 recognized their epitopes only when **SCF** was at least partially denatured. mAb 7H6 was found to neutralize in vitro **SCF** -mediated cell proliferation and **SCF** binding to its receptor, when present in equimolar concentrations relative to the ligand, suggesting that the epitope region is functionally significant. Evidence that the mAb 7H6 epitope is represented by discontinuous regions (residues within sequences 61-65 and 91-95 are critically involved) is presented. The observation that the mAb 7H6 epitope is discontinuous has implications for the **structure** of **SCF** .

10/AU,TI,SO,AB/3 (Item 3 from file: 76)

Human stem cell factor dimer forms a complex with two molecules of the extracellular domain of its receptor, Kit
Philo, J.S.; Wen, Jie; Wypych, J.; Schwartz, M.G.; Mendiaz, E.A.; **Langley,**

K.E.
J. BIOL. CHEM. vol. 271, no. 12, pp. 6895-6902 (1996)

Stem cell factor (**SCF**) is a cytokine that is active toward hematopoietic progenitor cells and other cell types, including germ cells, melanocytes, and mast cells, which express its receptor, the tyrosine kinase, Kit. **SCF** exists as noncovalently associated dimer at concentrations where it has been possible to study its quaternary **structure** it stimulates dimerization and autophosphorylation of Kit at the cell surface. We have used recombinant versions of human **SCF** and human Kit extracellular domain (sKit) to study **SCF** -Kit interactions. By size exclusion chromatography, plus various physical chemical methods including light scattering, sedimentation equilibrium, and titration calorimetry, we demonstrate the formation of complexes containing a dimer of **SCF** (unglycosylated **SCF** super(1-165)) plus two molecules of sKit. The concentrations of **SCF** and sKit in these studies were in the range of 0.35-16.2 mu M. The data are analyzed and discussed in the context of several possible models for complex formation. In particular, the sedimentation data are not consistent with a model involving cooperative binding. The K sub(d) estimate for **SCF** -sKit interaction, obtained by sedimentation equilibrium, is about 17 nM at 25 degree C. With glycosylated **SCF** super(1-165), the K sub(d) is considerably higher.

10/AU,TI,SO,AB/4 (Item 4 from file: 76)

Amino acid sequence and post-translational modification of stem cell factor isolated from Buffalo rat liver cell-conditioned medium.
Lu, Hsieng S.; Clogston, C.L.; Wypych, J.; Fausset, P.R.; Lauren, S.; Mendiaz, E.A.; Zsebo, K.M.; **Langley, K.E.**
J. BIOL. CHEM. vol. 266, no. 13, pp. 8102-8107 (1991.)

Stem cell factor (**SCF**) isolated from culture medium conditioned by Buffalo rat liver cells was subjected to detailed structural analysis. Attempts at direct N-terminal sequencing of the factor indicated that its N terminus is blocked as pyroglutamic acid. The factor as isolated is a single polypeptide of 164 or 165 amino acids. The sequence is confirmatory to a sequence deduced from a cDNA sequence and provides important evidence for C-terminal processing of the polypeptide encoded by cDNA.

DIALOG-BIOTECH

S1	14708	SCF AND STRUCTURE
S2	109	S1 AND (THREE(W)DIMENSIONAL)
S3	9	S2 AND (ACTIVE OR HOT)
S4	25	S2 AND BIND?
S5	17	RD (unique items)
S6	30	S2 AND CRYSTAL
S7	27	RD (unique items)
S8	3	S7 AND DESIGN
S9	9	S3
S10	9	RD (unique items)
S11	1	S6 AND STEM
S12	22122	STEM(W)CELL(W)FACTOR
S13	23	S12 AND ((THREE(W)DIMENSIONAL)(W3)STRUCTURE)
S14	81	S12 AND CRYSTAL
S15	3	S14 AND (ACTIVE(W)SITE)
S16	3	RD (unique items)
S17	0	S23 AND ACTIVE(W)SITE
S18	1	S13 AND (ACTIVE(W)SITE)

DIALOG-BIOTECH

S1	14708	SCF AND STRUCTURE
S2	109	S1 AND (THREE(W)DIMENSIONAL)
S3	9	S2 AND (ACTIVE OR HOT)
S4	25	S2 AND BIND?
S5	17	RD (unique items)
S6	30	S2 AND CRYSTAL
S7	27	RD (unique items)
S8	3	S7 AND DESIGN
S9	9	S3
S10	9	RD (unique items)
S11	1	S6 AND STEM